



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,741	12/04/2001	Joseph Herman Krushinski JR.	X-11704	7715

25885 7590 10/24/2003
ELI LILLY AND COMPANY
PATENT DIVISION
P.O. BOX 6288
INDIANAPOLIS, IN 46206-6288

EXAMINER

BERCH, MARK L

ART UNIT PAPER NUMBER

1624

DATE MAILED: 10/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/890,741	Applicant(s) KRUSHINSKI ET AL.	
	Examiner Mark L. Berch	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 September 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10, 14-18 and 20-29 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 14-16, 20-25 is/are allowed.
- 6) ☒ Claim(s) 1, 2, 4, 5, 10 and 26-29 is/are rejected.
- 7) ☒ Claim(s) 6-9, 17 and 18 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/22/2003 has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 28 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 28, it is not clear what actual process "neuronal protein extravasation" refers to. A search on the PubMed data base did not find this phrase. In response to a request to submit a scientific article on the subject, applicants tendered two references. The examiner cannot locate this phrase in either reference, and applicants did not state where the phrase was present. The further traverse is unpersuasive. Applicants assert that they "can be their own lexicographer in drafting a specification." But applicants did not do that. This term did not exist in the art, and they did not define it in the specification. Instead, they make a statement in the remarks that "neuronal protein extravasation" means the same thing as "dural protein extravasation", a term which they

Art Unit: 1624

locate in one of the two references. Even leaving aside the fact that this particular reference does not define "dural protein extravasation", on what basis was this statement possibly made? It doesn't even make sense. For "dural protein extravasation" and "neuronal protein extravasation" to be the same thing, then "dural" would have to be the same as "neuronal". But these are totally different.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

There is a stray "I;" which is superimposed on the formula in claim 1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 2, 4, 5, 10, 26-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carr.

Note formula I for the final products. Note also Formula IV in column 4 for the intermediate, corresponding to R=H. These embrace applicants compounds. The final product species appear in the paragraph bridging columns 2-3. Note species 1 and others. For the N-H species, note column 15, lines 13-14 and Example 3, These differ only in that they have the acetamido, or sulfonamido substituent at the 4 position on the benzene ring (para) while applicants have it at the 3-position (meta). However, the

Art Unit: 1624

Formula I and Formula IV drawings clearly show the other positions as well. In addition, it is well established that position isomers, even without the floating valence, are *prima facie* structurally obvious even in the absence of a teaching to modify. The isomer is expected to be preparable by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing the position isomers. This circumstance has arisen many times. See: *Ex parte Englehardt*, 208 USPQ 343, 349; *In re Mehta*, 146 USPQ 284, 287; *In re Surrey*, 138 USPQ 67; *Ex Parte Ulliyot*, 103 USPQ 185; *In re Norris*, 84 USPQ 459; *Ex Parte Naito*, 168 USPQ 437, 439; *Ex parte Allais*, 152 USPQ 66; *In re Wilder*, 166 USPQ 545, 548; *Ex parte Henkel*, 130 USPQ 474; *Ex parte Biel*, 124 USPQ 109; *In re Petrzilka*, 165 USPQ 327; *In re Crownse*, 150 USPQ 554; *In re Fouche*, 169 USPQ 431; *Ex parte Ruddy*, 121 USPQ 427; *In re Wiechert*, 152 USPQ 249, *In re Shetty*, 195 USPQ 753.

For example, “Position isomerism has been used as a tool to obtain new and useful drugs” (*Englehardt*) and “Position isomerism is a fact of close structural similarity” (*Mehta*, emphasis in the original). See also MPEP 2144.09, second paragraph.

Claims 1-5, 10, 26-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Butera, Oinuma, or Helsley, alone or in view of Carr.

In Butera, note that A can be pyridyl. In Oinuma, note that Y is broadly defined, with many species having aralkyl or heteroaryl-alkyl. See e.g. Column 24 line 12, example 2-6, 10-14, 18-19, species at column 34, line 57, example 21, etc. In Helsley, the species have R1 as OH. See Example 8A, 8B, 13B, 13C. The same reasoning applies. In addition, Carr teaches that the substituent on the benzoyl can be at other positions.

The declaration is unpersuasive. The compounds tested, 2 and 4, do not appear in Carr. First, the compounds of Carr have either an aralkyl group on the piperidine N, or a hydrogen. These tested have methyl. Second, the compounds of Carr are either acetamides or sulphonamides. These tested are halogenated benzamides. Likewise for the other references. The compounds tested against are not in the prior art, or at any rate are not in the references over which the rejection is made. Comparative showings must be done against the closest prior art cited, Cf. *In re Merchant*, 197 USPQ 785, 788; *In re Zeidler*, 215 USPQ 490; *In re Holladay*, 199 USPQ 516, 518; *In re Malagari*, 182 USPQ 549, 553; *In re Baxter Travenol Labs*, 21 USPQ2d 1281; *In re Burkel*, 201 USPQ 67; *In re Chapman*, 148 USPQ 711, 715.

The newest traverse is unpersuasive. Applicants argue that a prima facie case has not been made. Applicants argue that none of the cited references teach or suggest 5-HT_{1F} agonist activity. The fact that the prior art compounds are not disclosed to have this particular mode of action is not enough to avoid an obviousness rejection. Applicants must show that the prior art compounds do not actually have the property disclosed here, by suitable comparative testing. Cf *In re Dillon*, 16 USPQ2nd 1897, 1901; *In re Hoch*, 166 USPQ 406; *Brown v. Gottshalk*, 179 USPQ 65; *In re Murch*, 175 USPQ 430. Note also *In re Lintner*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972). It is not necessary for the prior art to have recognition or appreciation of this activity for other than method of use claims. See also *In re Shetty*, 195 USPQ 753 for a case where the prior art did not teach applicants' exact utility. Note also *In re Baxter Travenol Labs*, 21 USPQ2d 1281, 1285 which states, "Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention." Note also *In re Ona*, 38

Art Unit: 1624

USPQ2d 1597 (“...all benefits need not be explicitly disclosed to render the claims unpatentable...”). That is, mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention, *In re Wiseman*, 596 F.2d 1019, 201 USPQ 658 (CCPA1979) “The fact that appellant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious.” *Ex parte Obiaya*, 227 USPQ 58, 60 (Board held asserted advantage would flow naturally from following the suggestion of the prior art.).

Applicants, citing *Lalu*, argue that intermediate cannot be used to render obvious. But the references teach final products. For example, Carr’s Formula I is a final product which is used for relief of pain, which incidentally is one of applicant’s uses as well, even if it arises via a different mechanism.

Applicants argue that the expectation of similar properties has been overcome by their declaration. This burden has not been met. The declaration has shown that there is unpredictability for applicants’ utility, but applicants, if they do not test the actual species of the prior art, must show unpredictability in the prior art utility, not applicants’ own utility. Further, as noted above, the compounds which applicants allegedly show unpredictability are simply not the compounds of the prior art; they have too many differences. Finally, even the reasoning were accepted, it would only eliminate the rejection of claims 1, 2, 4, 5, 10, 26-29 over Carr; it would not eliminate the other rejection.

Art Unit: 1624

Applicants also cite the section of the MPEP about failure of a reference to “teach any specific or significant utility”, but the references relied on all have a specific and significant utility.

Claims 6-9 and 17-18 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

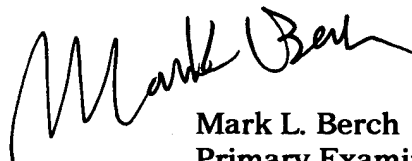
All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, THIS ACTION IS MADE FINAL even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Berch whose telephone number is 703-308-4718. The examiner can normally be reached on M-F 7:15 - 3:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 308-4716. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Art Unit: 1624

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 708-308-1235.

A handwritten signature in black ink, appearing to read "Mark L. Berch". The signature is fluid and cursive, with the first name "Mark" being more prominent than the last name "Berch".

Mark L. Berch
Primary Examiner
Art Unit 1624

October 21, 2003